

CLAIMS

1. A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence in a first entity, comprising the steps of: (a) preparing a reaction solution including the agent to be tested and a first entity including a bacterial RNAP homologous RNA-exit-channel amino-acid sequence; and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the homologous bacterial RNAP RNA-exit-channel amino-acid sequence.

2. The method of claim 1 wherein the first entity is an intact bacterial RNAP.

3. The method of claim 1 wherein the first entity is a fragment of a bacterial RNAP.

4. The method of claim 1 wherein the first entity is *Escherichia coli* RNAP or a derivative thereof.

5. The method of claim 1 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

6. The method of claim 1 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

7. The method of claim 6 wherein the second entity is a derivative of an intact bacterial RNAP.

8. The method of claim 6 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

9. The method of claim 6 wherein the second entity is a derivative of *Escherichia coli* RNAP.

10. The method of claim 6 wherein the second entity is a derivative of *Bacillus subtilis* RNAP.

11. The method of claim 1 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to a eukaryotic RNAP derivative.

12. The method of claim 11 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

13. The method of claim 11 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

14. A method for identifying an agent that inhibits an activity of a bacterial RNAP by binding to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, comprising: (a) preparing a reaction solution comprising the agent to be tested and a first entity containing a bacterial RNAP homologous RNA-exit-channel amino-acid sequence; and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of inhibition of an activity of said first entity, wherein inhibition involves binding of the agent to the homologous bacterial RNAP RNA-exit-channel amino-acid sequence.

15. The method of claim 14 wherein the first entity is an intact bacterial RNAP.

16. The method of claim 14 wherein the first entity is a fragment of a bacterial RNAP.

17. The method of claim 14 wherein first entity is *Escherichia coli* RNAP or a derivative thereof.

18. The method of claim 14 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

19. The method of claim 14 wherein the activity is transcription initiation.

20. The method of claim 14 wherein the activity is transcription elongation.

5 21. The method of claim 14 wherein the activity is σ binding.

22. The method of claim 14 wherein the activity is NTP binding.

10 23. The method of claim 14 wherein the activity is DNA binding.

24. The method of claim 14 wherein the activity is RNA binding.

25. The method of claim 14 wherein the activity is open-complex formation.

15 26. The method of claim 14 wherein the activity is RNA synthesis.

27. The method of claim 14 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the inhibition by
20 the agent of the activity of a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

28. The method of claim 27 wherein the second entity is
25 a derivative of an intact bacterial RNAP.

29. The method of claim 27 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

30. The method of claim 27 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

30 31. The method of claim 27 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

32. The method of claim 27 wherein the activity is transcription initiation.

33. The method of claim 27 wherein the activity is transcription elongation.

5 34. The method of claim 27 wherein the activity is open-complex formation.

35. The method of claim 27 wherein the activity is NTP binding.

10 36. The method of claim 27 wherein the activity is DNA binding.

37. The method of claim 27 wherein the activity is RNA binding.

38. The method of claim 27 wherein the activity is open-complex formation.

15 39. The method of claim 27 wherein the activity is Gre-RNA synthesis.

40. The method of claim 27 wherein inhibition of an activity of the first entity and inhibition of an activity of the second entity are assessed sequentially.

20 41. The method of claim 27 wherein inhibition of an activity of the first entity and inhibition of an activity of the second entity are assessed simultaneously.

42. The method of claim 14 further comprising comparison of: (a) at least one of the presence, extent, 25 concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

30 43. The method of claim 42 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

44. The method of claim 42 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

45. The method of claim 14 wherein at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity also is compared to at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by an inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence of an activity of the first entity.

46. A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, comprising (a) preparing a reaction solution comprising the agent to be tested, a first entity containing a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, and containing a detectable group within σ region 3.2; and (b) detecting a change in a property of the detectable group within σ region 3.2.

47. The method of claim 46 wherein the first entity is an intact bacterial RNAP.

48. The method of claim 46 wherein the first entity is a fragment of a bacterial RNAP.

49. The method of claim 46 wherein the first entity is *Escherichia coli* RNAP or a derivative thereof.

50. The method of claim 46 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

51. The method of claim 46 wherein the reference compound contains a chromophore.

52. The method of claim 46 wherein the detectable group contains a fluorophore.

53. The method of claim 46 further comprising measurement of FRET.

54. The method of claim 46 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

55. The method of claim 54 wherein the second entity is a derivative of an intact bacterial RNAP.

56. The method of claim 54 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

57. The method of claim 54 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

58. The method of claim 54 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

59. The method of claim 46 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

60. The method of claim 59 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

61. The method of claim 59 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

62. A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, comprising (a) preparing a reaction solution comprising the agent to be tested, a reference compound that

binds to a homologous bacterial RNAP RNA-exit-channel amino-acid sequence, and a first entity containing a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of competition by the agent for binding of the reference compound to the homologous RNA-exit-channel amino-acid sequence.

63. The method of claim 62 wherein the first entity is an intact bacterial RNAP.

64. The method of claim 62 wherein the first entity is a fragment of a bacterial RNAP.

65. The method of claim 62 wherein the first entity is *Escherichia coli* RNAP or a derivative thereof.

66. The method of claim 62 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

67. The method of claim 62 wherein the reference compound contains a detectable group.

68. The method of claim 62 wherein the detectable group contains a chromophore.

69. The method of claim 62 wherein the detectable group contains a fluorophore.

70. The method of claim 62 wherein the reference compound is a chromophore-labeled inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence.

71. The method of claim 62 wherein the reference compound is a fluorophore-labeled inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence.

72. The method of claim 62 further comprising measurement of FRET.

73. The method of claim 62 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

74. The method of claim 73 wherein the second entity is a derivative of an intact bacterial RNAP.

75. The method of claim 73 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

76. The method of claim 73 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

77. The method of claim 73 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

78. The method of claim 62 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

79. The method of claim 78 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

80. The method of claim 78 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

81. The method of claim 62 wherein at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the first entity is compared to at least one of the presence, extent, concentration-dependence, or kinetics of binding of an inhibitory compound specific to

the bacterial RNAP homologous RNA-exit-channel amino-acid
sequence to the first entity.